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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/832,233
Filing Date: April 10, 2001
Appellant(s): KINK ET AL.

Peter G. Carroll
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 29, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

For the sake of clarity, the statement of the rejection at issue, at page 2 of the Final Office Action mailed on July 01, 2004 ("Final Rejection"), inadvertently contains a typographical error. Accordingly, the statement rejects claims 1-5, 9-14. However, all other parts of the Final Rejection, specially the Summary of the Office Action and the Conclusion section, clearly indicate that all claims; namely, claims 1-5, 7-14, were subject to the obviousness rejection instantly at issue.

In fact, Appellant's Arguments submitted in the Brief confirms that Appellant was on full notice about all the claims 1-5, 7-14 being subject to the obviousness rejection at

issue. Therefore, as recognized by the Appellant, the issue before the Board is whether the rejection of the claim 1-5, 7-14 under 35 U.S.C. 103(a) is proper.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-5, 7-14 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,656,272	Le et al	8-1997
5,833,984	Eibl et al	11-1998
5,601,823	Williams et al	02-1997

- Eible et al. Prevention of Necrotizing Enterocolitis in Low-Birth-Weight Infants by IgA-IgG Feeding. N Eng J Med 1988; 319: 1-7
- Wolf et al. The Anti-Inflammatory Effect of an Oral Immunoglobulin (Ig-A-IgG) Preparation and its Possible Relevance for the Prevention of Necrotizing Enterocolitis. Acta Paediatr Supp 1994; 396: 37-40
- Muguruma et al Role of Platelet Activating Factor in Necrotizing Enterocolitis Development in the Rat. Prenat Neonat Med 1998; 3: 571-579.

(10) Grounds of Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1-5, 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Le et al US Patent 5,656,272, Eibl et al US Patent 5,833,984 ("Eibl II") in view of Wolf et al, (Acta Pediatr. supp. 1994, 396, 37-40), Muguruma et al (Prenat Neonat Med 1998;3:571-579), Eibl I (Acta Pediat 83,666-668, 1994) and Williams et al US Patent 5,601,823.

Le teaches anti-TNF antibodies for treating inflammatory bowel diseases such as Crohn's disease (see abstracts, examples 1-3, 21; col 66-col 68, claims 1-10). Le fails to specifically teach anti-TNF use for treating Neonatal Necrotizing Enterocolitis (NEC).

Eibl II discloses methods of using anti TNF- antibodies to reduce the inflammatory response caused by gram-negative bacterimia (col 2, lines 7-10). Eibl further teaches the correlation between levels of TNF and the pathogenesis of neonatal NEC (see col 1, lines 60-66). Eibl further teaches various modes of administration of

antibodies to a patient (col 6, lines 5-20). Eibl fails to specifically use anti-TNF antibodies in treating NEC.

The role of TNF in the development of neonate NEC has been well established in the art. Accordingly, Wolf, Eibl I and Muguruma are merely used to set forth general knowledge in the art about TNF and NEC.

Wolf, for example, describes the general knowledge about the affects of oral IgA-IgG preparations in inhibiting TNF release thereby preventing the development of pathological changes associated with NEC in low-birth-weight infants (p. 667, 4th para).

Eibl I sets forth successful use of IgA-IgG in treating or preventing NEC among human infants (see abstract, discussion).

Muguruma also teaches the role of TNF in the pathogenesis of NEC and ultimately the development of said condition specifically in low-birth-weight neonates (see abstract, entire document). Muguruma indicates the important role of pro-inflammatory agents such as TNF (page 575, 2nd, 3rd para-page 576, 2nd para.). Muguruma et al, however, fails to specifically teach the use of antibodies directed to TNF as a means of decreasing TNF activity among susceptible patients.

Eibl, Maguruma, and Wolf teach methods of treating conditions that are caused by over expression of pro-inflammatory factors, therefore, their teachings are viewed as being in the same field of endeavor.

Williams is merely used to show the state of art in formulating polyclonal avian antibodies for treating inflammatory enterocolitis caused by *Clostridium difficile*. (see abstract, col 21-col 24). Williams provides to one of ordinary skill in the art adequate

teachings to prepare antibodies for treatment of gastric inflammatory diseases similar to NEC. Neonates or infants can use the formulation of Williams. (see claim 3, col 1, line 44). Williams displays various advantages in using avian antibodies for oral administration. (col 9-11).

The role of TNF as a pro-inflammatory mediator in development of NEC has been well established in the art as shown by Maguruma, Wolf and Eibl I. Therefore, even though Le does not explicitly disclose the use of anti-TNF antibodies in treating NEC in neonates, it would have been obvious to one of ordinary skill in the art at the time of invention to employ such products for treatment of NEC, because as suggested by Eible II, Muguruma and Eibl I and Wolf, TNF plays an integral role in development of NEC and the ordinary skill in the art would have had a reasonable expectation of success in employing the anti-TNF of Le for treating NEC.

Furthermore, one of ordinary skill in the art would have been motivated to formulate an avian polyclonal anti-TNF, because as suggested by Williams such type of antibodies can be administered orally are non-immunogenic and are well tolerated by infants.

Additionally, it is well established that TNF potentiates the progress of NEC, thus reducing the effects of TNF activity among human infants would improve or alleviate the pathological changes that would lead to NEC. Examiner states that any degree of relief from NEC would read on the scope of the instant claims, and the ordinary skill in the art

would have had a reasonable expectation of success in at least observing some symptomatic relief when administering the anti-TNFs taught by [*sig*. Eibl] Le[1].

(11) Response to Argument

Appellant's arguments on the Brief filed on November 24, 2004 ("Brief") have been fully considered but they are not persuasive.

Appellant argues that Examiner's conclusion does not meet the *Prima Facia* standards of Obviousness because (I) the cited prior art references do not teach "an Anti-TNF Antibody" for treating "Necrotizing Enterocolitis," (II) the cited references provide no motivation to combine, and (III) the references do not teach any reasonable success

In response Examiner states that contrary to Appellant's position (I) the rejection properly describe the claimed invention, because all elements of the instant claims are described by the combined teachings of the references, (II) the state of art as described by the cited reference provide ample suggestion and motivation to modify the references as described on record, and (III) one of ordinary skill in the art in possession of the cited references would have had a reasonable expectation of success to reach the claimed invention.

Thus, for the reasons set forth below the Board of Appeals and Interferences ("the Board") should affirm the rejection of record.

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[1] The Office Action contains a typographical error by attributing the teachings of anti-TNF to Eibl. However, it is clear from the entire body of the rejection that the last word on this rejection should have been "Le" not "Eibl. Attention of The Board is directed to pages 17-19 of this Examiner's Answer for clarification of this typographical error.

Please note that Examiner's response to Appellant's arguments parallels the same sequence as presented by the Appellant. Thus, any issue that is not raised by the Appellant is viewed to be moot.

I. The Board should affirm the rejection because contrary to Appellant's arguments the combined teachings of the references meet all elements of the instant claims

Appellant argues that the references do not teach "An Anti-TNF Antibody" for treating NEC (*see* Brief at page 9). Examiner does not find this reasoning persuasive, because the rejection is made under the obviousness standard set forth in. *Graham* **v.** *John Deere Co.*, 383 U.S. 1. Accordingly, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Had any of the references, in fact, by itself taught an anti-TNF antibody for treating NEC, the rejection would have been made under the 35 USC 102. Here, it is the combined teachings of references that render the instant claims obvious.

The scope of the instant claims are directed to methods of treatment for NEC comprising providing a patient with symptoms of NEC and then administering a formulation comprising purified anti-TNF polyclonal antibodies to said patient. The Final Rejection specifically clarifies Examiner's position that any relief from NEC, subsequent to the anti-TNF administration, would read on the scope of the instant claims. (*see* Final Action at page 4, last para). The combined teachings of the references meet all such limitations.

First, Appellant has apparently misinterpreted the Examiner's factual findings as enumerated by the *Graham v. Deere* Court. At page 9 of the Brief, Appellant states that Examiner admits that Le et al does not teach an anti-TNF antibody. (*see* page 9, 3rd para under the heading C). However, such interpretation by Appellant is simply not correct, because as described at page 2 of the Final Action, Examiner stated "Le teaches anti-TNF antibodies for treating inflammatory bowel diseases such as Crohn's disease." At col 68, lines 17-20, Le teaches that his anti-TNF antibodies provide successful treatment tf TNF related pathologies, as exemplified by Crohn's disesase in human patients. Thus, Le clearly teaches anti-TNF antibodies for use in TNF related pathologies.

Appellant has misinterpreted Examiner's statement as it was made in relation to treating NEC. A fair reading of the statement in the Final Rejection clarifies this point. The statement says "Le fails **to specifically teach anti-TNF use for treating Neonatal Necrotizing Enterocolitis**." Indeed, had Le taught his anti-TNF antibodies for treating NEC, the rejection would have been made under 35 USC 102. The statement is a mere acknowledgement of the shortcomings of Le. However, the secondary references provide ample motivation and expectation of success that such anti-TNF antibodies can be used for treatment of NEC.in its avian form for patients in need.

For example, the Eibl II reference provides that etiologically NEC patients have high levels of TNF-α, ("TNF"). Eibl II suggests that TNF is involved in the pathogenesis of NEC (*see* col 1, lines 60-65). Eibl II also describes that TNF play a central role in human inflammatory response and anti-TNF antibodies have been shown to prevent

progression of responses (*see* col 1, lines 36-52; col 2, lines 5-15). Eibl (II) then describes other agents such as IgA and IgG which can reduce TNF-mediated inflammatory response by reducing TNF release. (see col 8, lines 1-5; col 10, line 65-col 12, line 66). Thus, Eible II shows that using anti-TNF compounds, such as IgA or IgG, reduce TNF induced inflammatory responses.

It is Examiner's position that one of ordinary skill in the art in possession of Le and Eibl II would have been motivated to also use the anti-TNFs of Le for treatment of TNF-induced NEC. Therefore, the general concept of administering anti-TNF antibodies for treatment of NEC is rendered obvious in view of Le and Eibl II.

The other references, Wolf, Muguruma, Eibl I and Williams are submitted as further evidence to show the general knowledge in the art about the role of TNF in the development of neonate NEC and the conventional modes of preparing avian antibodies for different modes of delivery. Thus, all limitations of the instant claims have been described by the combined teachings of the references.

Appellant also argues that the examiner has combined an excessive number of references and that is an indicator of nonobviousness. (*see* Brief at page 6, 4th para and footnote 1). In response, Examiner does not find this line of reasoning persuasive. Aside from the fact that Examiner does not find Appellant's legal basis for such assertion on the Brief; Examiner replies that reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Appellant then argues that Examiner has improperly employed an "invitation to try" analysis which is forbidden by the Federal Circuit as ruled *in In re O'Farrell*, 853 F.2d 894, 903; 7 USPQ2d 1673, 1681 (Fed Cir 1988). (*see* Brief at page 10, lines 1-2).

In response Examiner states that such line of reasoning is not persuasive, because analogous to the *In re O'Farrell*, the correct question here is: when is an invention that is obvious to try nevertheless obvious? As reasoned in *In re O'Farrell*, the "obvious to try" has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention. *Id.*

However, neither of these situations applies here. Using anti-TNF antibodies for TNF-mediated diseases have been well described in the art as evidenced in Le's Patent. Further, the role of TNF in pathogenesis of NEC has been well described as evidenced in Eibl, Wolf and Muuruma. There exists no varying of "all parameters" or "trying numerous possible choices among many parameters." All that is required here is mere application of Le's anti-TNF antibodies to another TNF mediated inflammatory disease such as NEC.

Moreover, the art of developing avian antibodies is well developed in the art as shown by Le and Williamson. Therefore, there is no requirement to develop a new technology or undergo extensive experimentation to prepare avian anti-TNF formulations of Le's antibodies.

It is well settled that obviousness does not require absolute predictability of success. Here, the combined teachings of the references provide such level of predictability. Appellant has not provided any evidence to show otherwise. Therefore, Appellant has not met their burden of persuasive and the Board should affirm the rejection.

Appellant also argues that Eibl II teaches that NEC immunotherapy does not involve direct neutralization by specific antibodies such as anti-TNF antibody. (*see* Brief at page 10, 3rd para.). Aside from the fact that it is not clear what is meant by the phrase "direct neutralization," because neither the specification nor the art teach such activities for any antibodies, Examiner points out that such line of arguments are not commensurate with the scope of the claims. None of the instantly pending claims require a direct neutralization step accomplished by anti-TNF antibodies. In fact, the therapeutic formulations employed in the instant claims use the inclusive "comprising" transitional language allowing additional therapeutic modalities. Thus, such line of arguments is not found persuasive.

II. The teachings of the references provide ample motivation for use of Le's anti-TNF antibodies for treatment of NEC.

Appellant further argues that Examiner has pointed to no statement in any of the references that suggests an antibody directed to a TNF antigen would be useful to treat NEC (*see* Brief at page 12, 2nd para).

In response Examiner states that again had such explicit teaching was provided in the form of an example in a given reference, the claims would have been rejected under the 35 USC 102. Here, the rejection is based on a proper obviousness analysis and the combined teachings of the references not only meet all elements of the instant claims, but also provide ample motivation in the art to use anti-TNF antibodies for treating NEC.

As the initial matter, the primary reference, Le, provide direct teachings about the nature of anti-TNF antibodies, including the polyclonal antibodies. The reference provides that such art have been well described in the art and are used to successfully treat various acute or chronic diseases with TNF-related pathologies. (*see* col 2 lines 28-col 6, line 40; col 34, lines 8-67). Le explicitly exemplifies the use of anti-TNF for treatment of Crohn's disease and suggests expectation of success for treatment of TNF related pathologies. (*see* col 68, lines 18-21). Thus, there is ample motivation provided by Le to use anti-TNF antibodies against TNF-mediated pathologies.

The secondary references are further employed to establish that NEC is a TNF-mediated disease. For example, Eible II explicitly states "high levels of TNF have also been found in neonates with NEC, suggesting that TNF may be involved in the pathogenesis of this disease." (see col 1, lines 61-65). Eible II further establishes

expectation of success by stating "endotoxin challenge and administration of TNF has induced bowel necrosis in an experimental model of NEC." (see col 1, lines 64-67). Eible II adds that the lethality of endotoxemia may be prevented by administration of specific anti-TNF antibodies. (see col 1, line 65-col 2, line 10). Such statements are viewed by Examiner to clearly provide motivation in the art that anti-TNF antibodies can be used for treatment of NEC.

All other secondary references are used to solidify this scientific position. Accordingly, Examiner had concluded that it would have been obvious to use Le's anti-TNF antibodies for treatment of other TNF-related pathologies including NEC, because the state of art provides such motivation to combine.

Second, Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, at least the general knowledge available to one of ordinary skill in the art provides the requisite degree of teaching, suggestion or motivation to combine the cited references.

Appellant first asserts that Eibl II teaches away from the instant claims. In response, Examiner states that Eibl at no place provides any teachings that amount to a direct teaching away from the instant claims. Appellant appears to misinterpret what it means to "teach away" from a patented invention.

"In general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the results sought by the applicant." *In re Gurley,* 31 USPQ2d 1130, 1131-2 (Fed. Cir. 1994). Here, the mere fact that there is an alternative means of reducing TNF activity in a TNF-mediated disease, as shown by Eibl II, does not does not preclude the use of the anti-TNF antibodies of Le for treating NEC.

In fact the portions of Eibl II patent that Applicant characterizes as a "teaching away," col 2, lines 24-27, does not discourage one of ordinary skill in the art to employ the anti-TNF antibodies of Le for treating NEC. On the contrary, Eibl II encourages the use of anti-TNF antibodies to reduce TNF activity and the lethality of endotoxemia which has been associated to the pathogenesis of NEC (*see* col 1, line 46-col 2, line 10).

Appellant then relying on *In re Rijcaert*, 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993), asserts that Examiner is NOT one skilled in the art and that a mere opinion of the Examine on what one skilled in the art might believe does not count. (*see* Brief at page 13, 2nd para.).

In response, Examiner states that the case of *In re Rijacert* is factually unrelated to the case at bar. In *Rijcaert* the claim limitation at issue, the relationship between three different variables, was somehow assumed to be "inherent" in the teachings of prior art without any scientific or legal basis. Here, unlike in *Rijacert*, Examiner has not assumed any claim limitations to be inherent among various variables. In fact, Examiner has relied on explicit teachings of the primary and secondary references to respectively show that anti-TNF antibodies are used to treat TNF-mediated diseases and that NEC

is a TNF-mediate disease. Thus, using anti-TNF to treat TNF would have been obvious. All secondary art would further solidify such reasoning and meet the additional elements of the instant claims.

Appellant, on the other hand,, has not met his burden of persuasion by coming forward with competent evidence or arguments to rebut the *prima facia* case of obviousness at issue. Appellant has simply not addressed the scientific conclusion and the legal rational behind the rejection. In fact, Examiner's factual statements and conclusion in the Final Rejection are left unchallenged.

Appellant has not provided any evidence that the anti-TNF antibodies of Le cannot be administered to patients having symptoms of NEC. Neither has Appellant provided any showing that anti-TNFs of Le are ineffective against NEC. Instead, Appellant has chosen to rely on numerous case rulings that are factually unrelated to the instant case. Accordingly, Appellant has not met the burden of persuasion and for such reasons set forth above the Board should affirm the rejection.

III. Contrary to Appellant's position, there is ample expectation of success to use anti-TNFs of Le for treatment of NEC.

Appellant argues that Examiner's statement about the Eibl II teachings of NEC treatment by anti-TNF is erroneous. (*see* Brief at page 13, 3rd para.). Accordingly, Appellant, relying on a typographical error, argues that it is Examiner who is making the conclusion that reducing the effects of TNF activity among human infants would improve or alleviate NEC, not one of ordinary skill in the art. (*Id.*)

In response Examiner states that Appellant's arguments should not be found persuasive, because Appellant appears to have selectively relied on a typographical error to support his erroneous conclusion. In fact, Appellant has ignored an entire page of reasoning in the Final Rejection, to establish that Eibl II does not teach NEC treatment by anti-TNF.

For the sake of clarity, the Final Action stating at page 4, last sentence states "... the anti-TNF taught by Eibl." should have read "...the anti-TNF taught by Le." Nevertheless, amid such typographical error, the Board should affirm the rejection because (a) Appellant was in full notice of the reasoning behind the pending rejection, and (b) Eibl in fact provides ample expectation of success for treating NEC with an anti-TNF.

(a) Appellant was in full notice of the reasoning behind the rejection

Appellant was in full notice of the reasoning behind the rejection because the entire pages 2- 4 of the Final Action mailed July 01, 2004 has diligently described the facts and the conclusion drawn to reject the pending claims.

Page 2 of the Final Action described the teachings of Le and EiblelI. Accordingly, Le was described to teach anti-TNF antibodies for treating inflammatory bowel diseases such as Crohn's disease and failed to specifically teach anti-ITNF use for treating NEC. Page 2 of the Final Action also described the teachings in Eibl II.

Accordingly,

> Eibl discloses methods of using anti TNF- antibodies to reduce the inflammatory response caused by gram-negative bacterimia (col 2, lines 7-10). Eibl further teaches the correlation between levels of TNF and the pathogenesis of neonatal NEC (see col 1 , lines 60-66). Eibl further teaches various modes of administration of antibodies to a patient (col 6, lines 5-20). **Eibl fails to specifically use anti-TNF antibodies in treating NEC.**

Thus, Examiner has acquiesced to the fact that Eibl II failed to use anti-TNF antibodies for treating NEC. The reliance on Eibl was on the col 1-2 statements about the use of anti-TNF antibodies to reduce inflammatory responses and the correlation between levels of TNF and the Pathogenesis of NEC. In fact, Appellant at page 10 of his Brief relied on the same statement to reason that Examiner was aware of Eibl II not teaching an anti-TNF antibody. (*see* Brief at page 10, 2nd para.). Therefore, Appellant was on full notice that the source of anti-TNF was not solely Eibl reference but also Le.

Page 3 of the Final Action goes on to establish that it is well described in the art that TNF plays an important role on the inflammatory process of NEC. Page 4 of the Final Action goes on to assert that the use of anti-TNFs of Le would have been obvious in view of the secondary references:

> The role of TNF as a pro-inflammatory mediator in development of NEC has been well established in the art as shown by Maguruma, Wolf and Eibl 1. Therefore, even though Le does not explicitly disclose the use of anti-TNF antibodies in treating NEC in neonates, it would have been obvious to one of ordinary skill in the ad at the time of invention to employ such products for treatment of NEC, because as suggested by Eible II, Muguruma and Eibl I and Wolf, TNF plays an integral role in development of NEC and the ordinary skill in the art would have had a reasonable expectation of success in employing the **anti-TNF of Le for treating NEC**. ...

A fair reading of the following paragraph at page 3 merely elaborate on the scope of the instantly pending claims and how the combined cited references would have rendered the scope of the instant claims obvious:

> Additionally, it is well established that TNF potentiates the progress of NEC and **thus reducing the effects of TNF activity among human infants would improve or alleviate the pathological changes that would lead to NEC**. Examiner states that **any degree of relief from NEC would read on the scope of the instant**

However, Appellant has selectively ignored the entire three pages of analysis

and relied on one typographic error to conclude that one of ordinary skill in the art would not have reached such conclusion. For such reasons the Board should affirm the rejection.

(b) Eibl in fact provides ample expectation of success for NEC treatment by an anti-TNF

In alternative to the rationales set forth above, Examiner points out that it would have been obvious to one of ordinary skill in the art at the time of invention to still had a reasonable expectation of success in reaching the instant claims when combining the teachings of Le, Eibl II, Wolf, Eibl I and Muguruma.

As reasoned, Le has explicitly taught that anti-TNF antibodies would have been effective against TNF-related inflammatory pathologies such as Crohn's disease. Accordingly, one of ordinary skill in the art would have been expected to turn to other references dealing with TNF-related diseases to practice other uses of Le's anti-TNF antibodies.

All secondary references provide scientific evidence that TNF plays an important role in causing NEC. Thus, Examiner's conclusion was based on a one of ordinary skill in the art interpretation of a reasonable expectation of success. Appellant has not provided any evidence to show otherwise. Thus, Appellant has not met the burden of persuasion to overcome the rejection.

The following ground(s) of rejection are applicable to the appealed claims:

Respectfully submitted,

Shahnam Sharareh, PharmD
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ss
April 20, 2005

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